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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,848	06/18/2001	Leona E. Ling	CIBT-P01-119	9957
28120	7590	04/07/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			YAEN, CHRISTOPHER H	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/883,848	LING ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Christopher H Yaen	1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 January 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-34 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. In view of the search burden imposed for the different inventions claimed in the instant application, the restriction requirement set forth in paper no. 1/13/2003 is hereby replaced with a new restriction requirement set forth herein.

### ***Election/Restrictions***

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:
- I. Claims 1-17, drawn to a method of promoting angiogenesis comprising the administration of an angiogenic amount of a peptide, classified in class 514, subclass 8. *If applicant elects this group for prosecution on the merits, applicant is required to select a single sequence from SEQ ID Nos: 1-20 and 26, this selection should not be construed as an election of species, see paragraph 8 below.*
  - II. Claims 1-2 and 25-27, drawn to a method of promoting angiogenesis comprising the administration of an angiogenic amount of an agonist, wherein the agonist is a small organic molecule, classified in class 514, subclass 66. *If applicant elects this group for prosecution on the merits, applicant is required to select a single agonist of the general formula (XII) (i.e. applicant must select specific variables for each of Ar, Ar', Y, X, M, R, CY, CY', i, and n), this selection should not be construed as an election of species, see paragraph 8 below.*

- III. Claims 18-20 and 22-24, drawn to a method of inhibiting angiogenesis comprising the administration of an anti-angiogenic amount of a hedgehog antagonist, wherein the antagonists is a polypeptide that binds to patched, classified in class 424, subclass 130.1.
- IV. Claims 18-19 and 21-24, drawn to a method of inhibiting angiogenesis comprising the administration of an anti-angiogenic amount of a hedgehog antagonist, wherein the antagonists is a polypeptide that binds to smoothened, classified in class 424, subclass 130.1.
- V. Claims 28-29, drawn to a method of promoting angiogenesis comprising the administration of a hedgehog nucleic acid molecule, classified in class 536, subclass 23.1. *If applicant elects this group for prosecution on the merits, applicant must select a single corresponding nucleic acid sequence, this selection should not be construed as an election of species, see paragraph 8 below.*
- VI. Claims 18 and 30-34, drawn to a method of inhibiting angiogenesis comprising the administration of an anti-angiogenic amount of a hedgehog antagonist, wherein the antagonist is a small organic molecule, classified in class 514, subclass 66. *If applicant elects this group for prosecution on the merits, applicant is required to select a single antagonist of the general formulas (I-XI). (i.e. applicant must select specific variables for each of the formulas), this selection should not be construed as an election of species, see paragraph 8 below.*

The inventions are distinct, each from the other because of the following reasons:

3. Inventions I-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions differ one from the other because the methods are used for different purposes and require the administration of different types of molecules. For example, Groups I-II, and V are methods of promoting angiogenesis but require the administration of different molecules such as proteins, organic molecules, or nucleic acids. Groups III-IV, and VI are drawn to methods of inhibiting angiogenesis but require the administration of different proteins and organic molecules. Groups I-II, and V differ from Groups III-IV, and VI because the methods are drawn to methods that reflect different spectrums of angiogenic modulation (i.e. either promoting or inhibiting).
4. Because these inventions are distinct for the reasons given above and the search required for Group I-VI are not required one for the other because the search would entail searches in different and distinct databases (i.e. protein database, nucleic acid database, and organic molecule databases) of which are not overlapping nor co-extensive, restriction for examination purposes as indicated is proper.
5. This application contains claims directed to the following patentably distinct species of the claimed invention:

In **group I**, an election of species is required for:

- i) chemical moiety (*polyalkylene glycol polymer, hydrophobic moiety, phosphate groups, acetyl groups, or sugar groups*);
- ii) angiogenic factors (*VEGF, HGF, bFGF, angiopoietin-1, angiopoietin-2, or MCP-1*).

In **groups III and IV**, an election of species is required for:

- i) disease condition (*malignant tumor, retinopathy, macular degeneration, nonmalignant tumor, rheumatoid arthritis, osteoarthritis, neovascular glaucoma, keloids, Crohn's disease, ulcerative colitis, or psoriasis*).

In **group V**, an election of species is required for:

- i) nucleic acid introduction method (*viral, lipofection, or naked DNA*).

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 8, 17, 24, and 29 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

8. Upon election of Groups I, II, V, or VI, Applicants are additionally required to elect a single Sequence identified by a specific sequence identification number or a single formula with specific and specified variables so as to construct a single and complete

organic molecule, which is identifiable by a specific chemical structure or name as indicated above as they apply to group(s). The recited sequences and formulas have different structures one from the other and the search for the sequences or formulas would be unduly burdensome. This requirement is not to be construed as a requirement for an election of species, since each of the sequence(s) or formula(s) recited in alternative form is not a member of a single genus of invention, but constitutes an independent and patentably distinct invention.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen



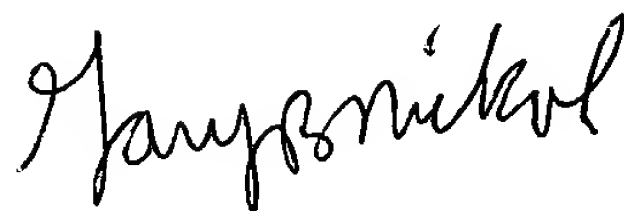
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March 31, 2004

A handwritten signature in cursive script, appearing to read "Gary Nickol".

**GARY NICKOL  
PRIMARY EXAMINER**